Remarks

A restriction requirement under 35 U.S.C. §§121 and 372 was set forth in the Official Action dated June 1, 2007 in the above-identified patent application.

At the outset, it is noted that a shortened statutory response period of one (1) month was set forth in the June 1, 2007 Official Action. Therefore, the initial due date for response was July 1, 2007. A petition for a two (2) month extension of time is presented with this response, which is being filed within the two month extension period.

It is the Examiner's position that claims 1-5, 7, 14-16, 18-24, 26-29, 31-32, 40, 46-47, 52, 54, and 56 in the present application are drawn to two (2) patentably distinct inventions which are as follows:

Group I: Claim(s) 1-5, 7, 14-16, 18-24, 26-29, 31-32, 40, 46-47, drawn to a method of inducing or promoting dopaminergic neuronal development.

Group II: Claim(s) 52, 54, 56, drawn to drawn to a method of obtaining a factor or factors which enhance proliferation, self-renewal, survival, and/or dopaminergic development, induction, differentiation, or maturation in a neural stem, progenitor, or precursor cell, or other stem or neural cell expression [*sic*] Nurr1 above basal levels.

Applicants respectfully disagree with the Examiner's position and submit that a withdrawal, or at the very least a modification, of the instant restriction requirement is clearly in order for the following reasons.

First, it is the Examiner's position that the inventions listed as Groups I - II do not relate to a single general

inventive concept under PCT Rule 13.1, because, under PCT Rule 13.2, they lack the same or corresponding special technical feature. In connection with this assertion, the Examiner contends that the art teaches that several genes, including Wnt1 and Nurr1, have been identified that control differentiation of dopaminergic and serotonergic neurons in the mid brain and the hind brain and cites Lee et al. for this premise. A careful review of Lee et al. reveals that the Examiner's reliance on this reference is misplaced. Applicants' novel method for inducing or promoting dopaminergic neuronal development in a stem, progenitor or precursor cell entails expressing a nuclear receptor of the Nurr1 subfamily above basal levels and then contacting the cells with a Wnt ligand. Claim 52 specifies similar method steps and further comprises isolating a growth factor or factors from such treated cells. Lee et al. are wholly silent as to the recited method steps for inducing or promoting dopaminergic neuronal development. Indeed, the methods of inducing differentiation described in Lee et al. entail culturing the cells in serum free medium with lacked basic fibroblast growth factor. See Johe et al. attached hereto which is cited in Lee et al. as describing the methods employed for inducing differentiation. The concept of over expressing a nuclear receptor of the Nurr1 subfamily in conjunction with stimulation with a Wnt ligand in order to stimulate such induction or promotion does not appear in Lee et al., nor in the references cited in Lee et al. Thus, it cannot reasonably be maintained that this reference teaches the special technical feature encompassed by the present claims.

Applicants respectfully submit that the Examiner's approach to unity is incorrect. On page 3 of the Official Action, the Examiner has acknowledged that the restricted groups share a relationship with each other "as they are similarly drawn to inducing or promoting neuronal development of dopaminergic

neurons." As discussed above, Applicants respectfully submit that the technical feature corresponding to each group of claims represents an advance over the prior art. Thus, the claims have unity.

The Examiner has alleged that the rules governing unity of invention state that only specific combinations will lead to a finding of unity of invention, and made the present restriction requirement on the basis that multiple products, multiple methods of using said products, and methods of making multiple products are present in the instant application. International Search and Preliminary Examination Guidelines are not part of the Rules of the PCT, and do not impose any requirements over and above the Rules of the PCT. These guidelines offer certain examples of where unity can clearly be acknowledged to be present. These examples are merely instances of where corresponding special technical features should be found to be present, and the guidelines are not exclusive; in other words, it would be incorrect to say that unity of invention can only be acknowledged for these examples. The fact that unity must be acknowledged in the situations identified by the Examiner at the top of page 3 of the Official Action does not mean that unity will be absent in other situations.

Applicants note that this is a PCT application, and the Examiner's citation to §1850 of the MPEP is in error since this section addresses unity of invention determinations before the International Searching Authority, not USPTO practice for separating claims to distinct inventions. According to §1850 of the M.P.E.P.: "it is clear that the decision with respect to unity of invention rests with the International Searching Authority or the International Preliminary Examining Authority." Applicants respectfully submit that during the international stage of this application the PCT Examiner did not make a lack of

unity finding and considered all of the claims to be directed to a single invention. Plainly, the instant restriction requirement fails to comply with the established USPTO practice of following the international rules regarding unity of invention in the prosecution of applications filed under 35 U.S.C. §371. While the Examiner purports to employ the general inventive concept practice under PCT Rule 13.1, it is wholly unclear how the Examiner could conclude that the instant application has two (2) groups of inventions with multiple species contained therein, when the PCT Examiner, employing the same rules, determined that identical claims in the international application have **complete unity** of invention. Accordingly, Applicants respectfully request the instant restriction requirement be withdrawn and all of the claims be examined on their merits.

Second, the only requirement for unity of invention is whether there is a single general inventive concept to the claims. A single general inventive concept will exist where there is the same or corresponding special technical feature. This is apparent from the fact that that only requirement set out in the Rules of the PCT governing how unity is assessed is Rule 13 PCT. Rule 13 PCT states that:

13.1 Requirement:

> The international application shall relate to one invention only or *to a group of inventions* so linked as to form a single general inventive concept ("requirement of unity of invention")(emphasis added).

13.2 Circumstances in Which the Requirement of Unity of Invention Is to Be Considered Fulfilled:

> Where a group of inventions is claimed in one and the same

international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

As mentioned above and acknowledged by the Examiner, the special technical feature is the inducement or promotion of dopaminergic neuronal development. This is achieved by 1) expressing a nuclear receptor of the Nurr1 subfamily above basal levels in the cell, and 2) treating the cell with a Wnt ligand. The combination of steps 1) and 2) is not taught by the prior art and is explicitly recited in both claims 1 and 52. Moreover, these steps define the contribution which each of the claimed inventions, considered as a whole, makes over the prior art in accordance with PCT Rule 13.2. In particular, Group I relates to expressing Nurr1 in cells above basal levels and treating the cells with a Wnt ligand and hence inducing or promoting dopaminergic neuronal development. The claims of Group II are directed to methods of obtaining factors which enhance proliferation, self-renewal, survival and/or dopaminergic development, induction, differentiation, or maturation in a neural cell. However, the initially recited process steps are identical to those recited in the Group I invention. Thus, the claims of Group I and II clearly relate to the same inventive concept which results in enhanced proliferation, self-renewal, dopaminergic induction, survival, differentiation, or maturation in a neural stem, progenitor or precursor cell, or other stem or neural cell.

Third, as stated in the M.P.E.P. at §1893.03(d):

> Examiners are reminded that unity of invention (not restriction) practice is applicable in international applications (both Chapter I and II) and in national stage applications submitted under 35 U.S.C. 371.
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> When making a lack of unity of invention requirement, the examiner must (1) list the different groups of claims and (2) explain why each group lacks unity with each other group (i.e., why there is no single general inventive concept) specifically describing the unique special technical feature in each group.
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> The principles of unity of invention are used to determine the types of claimed subject matter and the combinations of claims to different categories of invention that are permitted to be included in a single international or national stage patent application.
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> The basic principle is that an application should relate to only one invention or, if there is more than one invention, that applicant would have a right to include in a single application only those inventions which are so linked as to form a single general inventive concept.
>
> A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features refers to those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art.

Applicants note that some of the language above is recited in the PCT Rules.

Fourth, in the present case the Examiner contends that the two groups of invention require different and distinct steps from each other, yet acknowledges the presence of a relationship. Since unity is to be determined with regard to the Articles and Rules of the PCT, Applicants respectfully submit that if all of the claims share a special corresponding technical feature, then

they must be considered unified and should be allowable in one application. Additionally, Applicants respectfully submit that the examination of Groups I and II together cannot be reasonably regarded as imposing a serious burden on the Examiner since both groups are directed to the same inventive concept and the groups have a disclosed relationship as mandated by the M.P.E.P. In light of the fact that an equivalent search for the methods of the invention is required, Applicants submit that the Examiner's search burden would not be increased by searching the groups together. Art relating to the method of Group I would necessarily be coextensive with art relating to the methods of Group II and vice-versa.

At page 4 of the Official Action, the Examiner has indicated that the inventions be subjected to further restricted. Specifically, the Examiner states that one Nurr1 family member must be elected from claims 2 and 3. Additionally, the Examiner states that if Nurr1 is elected, Applicants must elect either nucleic acid or protein (claims 4 and 5) and further that DNA or RNA must be elected if Applicants elect Nurr1 nucleic acid. Applicants submit that this restriction is unsound, and respectfully submit that a requirement for an election of species is clearly more appropriate and consistent with the guidance provided in the M.P.E.P., if any type of restriction must be made at all. Indeed, should the Examiner maintain her position, a claim limited to delivery of DNA encoding a nuclear receptor of the Nurr1 subfamily could be readily avoided by a competitor via the delivery of an mRNA encoding the same protein molecule. This is manifestly unfair to applicants. Indeed, the only basis for restriction of a national phase of a PCT application is for non-unity in accordance with the PCT rules discussed above. Considering this special technical feature, the requirement to elect that the nuclear receptor of the Nurr1 family be restricted

to a nucleic acid or protein and the further requirement to specify that the nucleic acid be limited to DNA or RNA seems arbitrary. For example, in searching the prior art, the Examiner would be required to search whether it has been disclosed that one could induce or promote dopaminergic neuronal development by enhancing proliferation, self-renewal, dopaminergic induction, survival, differentiation, and/or maturation in a neural stem progenitor or precursor cell, or other stem or neural cell by 1)expressing a nuclear receptor of the Nurr1 subfamily above basal levels in the cell and 2) treating the cell with a Wnt ligand as discussed above. Upon a finding that this is in fact novel and nonobvious, there is no basis for restricting all the different species of compositions identified by the Examiner. Under a proper consideration of unity of invention (as opposed to restriction practice) there is no rationale for separating out claims to a nucleic acid. Applicants respectfully submit that the novel and inventive method represents the link between the groups of claims, and further constitutes a single inventive concept as required under PCT Rule 13.1.

The Examiner has also asserted that claim 16 is subject to further restriction for consisting "of distinctly [*sic*] compounds of retinoids." The M.P.E.P. at §803 states that "if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they may be directed to independent and distinct inventions." "Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. Should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended."

Applicants respectfully submits that with regard to claim 16, a requirement for an election of species is clearly more appropriate and consistent with the guidance provided in the MPEP than a restriction requirement, if any type of restriction must be made at all.

The Examiner has also restricted the growth factors and combinations of growth factors of claim 18 which may be administered to the cell and required a specific combination to be elected. Applicants disagree with this restriction and again submit that this would be more appropriate as an election of species because this is not a permissible restriction requirement under the PCT rules.

Likewise, the Examiner contends that the claims of Group I comprise many distinct methods. Specifically, claim 21 is allegedly drawn to methods that can be carried out *in vivo* or *in vitro* (Applicant must elect one), claims 20, 22-24, and 26-27 comprise distinctly named cells that can be co-cultured with the neural stem cells (Applicants must elect one), and claims 29, 31-32, 40, and 46-47 comprise distinct methods of using the cells (Applicant must elect one). The points made above regarding this further restriction of the individual claims also apply to claims 20-24, 26-27, 29, 31-32, 40, and 46-47 that have been restricted. Again, a species election is more appropriate here and the Examiner's requirements are inconsistent with the requirements of the PCT rules regarding restriction practice/unity of invention.

For all of the foregoing reasons, Applicants respectfully request withdrawal of the present restriction requirement. In order to be fully responsive to the instant restriction requirement, Applicants hereby elect, with traverse, Group I, namely claims 1-5, 7, 14-16, 18-24, 26-29, 31-32, 40, and 46-47 drawn to a method of inducing or promoting dopaminergic neuronal development. Regarding the requirement for further restriction,

which is strenuously traversed, Applicants hereby elect the following:

1) Nurr1 as the nuclear receptor (claim 2);
2) DNA encoding the Nurr1 nuclear receptor (claim 4);
3) an activator of retinoid X receptor (claim 16);
4) bFGF and FGF-8 and Shh as the combination of growth factors (claim 18);
5) methods to be carried out *in vitro* (claim 21);
6) early midbrain glial cells (claim 20);
7) treating a patient (claims 29 and 31);

Species elections:

1) Wnt 5a (claim 7)
2) antioxidant (claim 19)

Claims 1, 2, 4, 5, 7, 15, 16, 18, 19, 20, 21-24, 26, 28, 29, 31, 32, 40, 46 and 47 read on the elected invention.

Applicants' election in response to the present restriction requirement is without prejudice to their right to file one or more continuing applications, as provided in 35 U.S.C. §120, on the subject matter of any claims finally held withdrawn from consideration in this application.

Early and favorable action on the merits of this application is respectfully solicited.

Respectfully submitted,
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